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VITAMIN D SUPPLEMENTS AND EFFECT ON GLYCEMIC CONTROL AND LIPID PROFILE IN INDIVIDUALS LIVING WITH DIABETES: A RETROSPECTIVE STUDY

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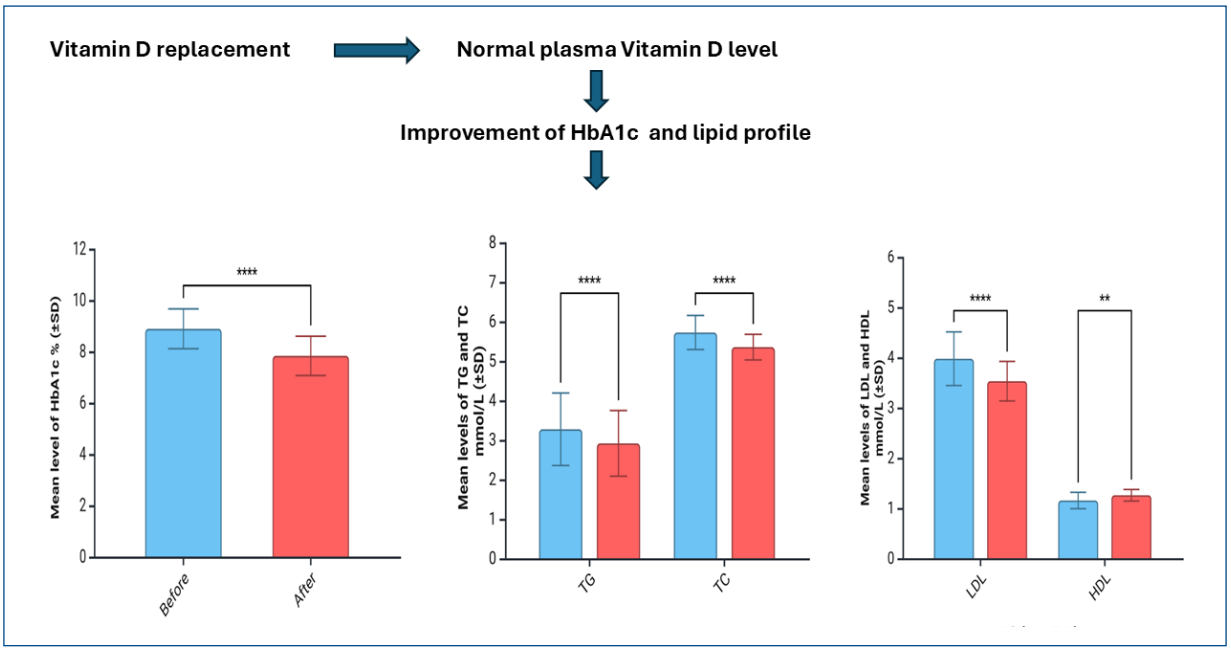
ABSTRACT – *Objective:* Diabetes Mellitus (DM) is a global concern with a high prevalence among the Saudi population. Uncontrolled diabetes is associated with serious medical complications and an increase in mortality and morbidity. Vitamin D deficiency may have the potential to decrease insulin sensitivity and alter lipid metabolism. This study aimed to assess the impact of vitamin D supplements on glycemic control and lipid profile among individuals living with diabetes in Saudia Arabia.

Materials and Methods: This retrospective study recruited 254 individuals with diabetes. The medical records were searched for age, gender, HbA1c, fasting blood glucose (FBG), Vitamin D and lipid profiles. The population records were extracted in two intervals: before taking vitamin D supplements and three months after receiving supplements. Paired t-test and confidence intervals were used to compare HbA1c, FBG, vitamin D, and other extracted variables between intervals. Vitamin D levels were compared between genders in each interval.

Results: The supplementation of vitamin D leads to improvement in vitamin D from a mean of 45.4 to 65 (normal reference range 50-150). Supplementation of vitamin D showed significant improvement in HbA1c, FBG, all parameters of lipid profile, renal and liver function and hemoglobin ($p < 0.001$) when *t*-test was used and confidence interval calculated.

Conclusions: Vitamin D plays a potential role in insulin sensitivity and lipid metabolism. Therefore, maintaining optimal level of vitamin D through its supplements or sun exposure might help to improve heath and decrease complications especially in individuals with diabetes.

KEYWORDS: Diabetes, Type 2 diabetes, HbA1c, Vitamin D, Supplement, Sun exposure, Vitamin D deficiency, Saudi Arabia.



Graphical Abstract. Vitamin D supplements improve glycaemic control and lipid profile in individuals living with diabetes. ****p-value <0.001; **p-value <0.01.

INTRODUCTION

The burden of Diabetes mellitus (DM) is well recognized across the globe, and this is likely due to an exponential increase in prevalence of type 2 diabetes[1]. The increase in the prevalence of obesity has been accompanied by a rise in metabolic dysfunction-associated steatotic liver disease (MASLD), a spectrum of liver conditions that includes simple steatosis and metabolic dysfunction-associated steatohepatitis (MASH). This condition can be associated with insulin resistance and lead to an increase in prevalence of type 2 diabetes[2]. According to the International Diabetes Federation (IDF), the number of individuals with diabetes will increase by 51% by the year 2045[3]. Therefore, it is not surprising that the prevalence of DM in Saudi Arabia was 17.7% in 2021[3,4]. Such increase in the prevalence of diabetes will put more pressure on Saudi Arabia health system, especially at primary care level.

In addition, a recent systematic review and meta-analysis[5] revealed a high prevalence of type 2 diabetes in Saudi Arabia, with a pooled prevalence of 16.4% (95% CI: 11.6-17.5) based on a total pooled population of 258,283. In addition, the study showed variation in diabetes prevalence in different geographical location of the Kingdom of Saudia Arabia, but higher prevalence among the older age groups[5]. Importantly, uncontrolled diabetes is associated with serious medical complications and an increase in mortality and morbidity, such as an increase in cardiovascular disease, diabetic retinopathy, diabetic nephropathy, stroke and peripheral vascular disease[6]. Poor adherence to diabetes medication is recognized as one of the reasons behind a high prevalence of poor diabetes control, and this is recognized as a common problem globally[7]. Vitamin D, besides its role in calcium and bone homeostasis, was shown to have a potential impact on the optimization of diabetes control and prevention of some diabetes complications[8]. In addition, the associations between vitamin D deficiency (< 50 nmol/L) and alterations in blood glucose and insulin levels were reported[9,10]. For instance, Abukanna et al[9] showed that three studies demonstrated that vitamin D deficiency (VDD) was a significant risk factor for developing T2DM, and one reported that it increased insulin resistance. However, they also showed that VDD did not affect the incidence of T2DM and the insulin sensitivity or glycated hemoglobin (HbA1c) levels in patients with T2DM[9]. Zhang et al[10] showed that oral vitamin D supplementation in individuals with prediabetes improved fasting insulin, blood glucose, and HbA1c levels. Moreover, long-term supplementation may help improve insulin resistance. Therefore, correcting vitamin D deficiency may help in reducing the prevalence of T2DM or at least improve glycemic control in individuals with diabetes. Importantly, Dadon et al[11] showed that no strong evidence was found to support the fact that vitamin D replacement may help in optimizing glycemic control in type 1 diabetes. The study by Dadon may raise questions about whether vitamin D is necessary in preservation of pancreatic insulin secretions, and whether in-

sulin itself may be a prerequisite for vitamin D to maintain the function of ß-cell in the pancreas[11]. However, the following studies showed that VDD in individuals with type 2 diabetes can be associated with poor glycemic control, hypertension, increase level of plasma uric acid and increase in the risk of diabetes complications. For instance, Albai et al[12] showed that low vitamin D can be associated with poor glycemic control, hypertension, diabetic neuropathy, cardiovascular disease and increased risk of dementia and cancer.

Several studies showed an association of vitamin D deficiency with an increase in plasma uric acid level, dyslipidemia and diabetic nephropathy[13-15]. In a systematic review and meta-analysis of 13 studies which included 3,850 control group and 1,797 as exposure group, Iqhrammullah et al[16] showed that that serum vitamin D level was significantly lower in patients with diabetes and cardiovascular diseases. The authors concluded that low vitamin D status can be regarded as a risk factor for cardiovascular disease which needed to be monitored[16]. Other scholars also suggested that the protective mechanism of vitamin D supplement is mediated through potential impact on gut microbiota profile as vitamin D may have prebiotic properties[17].

Alotaibi et al[18] showed that low vitamin D was associated with high HbA1c, LDL-cholesterol and lipid profile in Saudi population. Importantly, in previous studies, vitamin D deficiency was found to be associated with dyslipidemia. For instance, Lu et al[19] in a systematic review and meta-analysis of 20 randomized controlled trials, showed that vitamin D supplementation significantly improves serum high-density lipoprotein (HDL) and triglyceride (TG) levels, but does not improve low-density lipoprotein (LDL) or total cholesterol (TC) levels. An umbrella review of 25 meta-analyses by Radkhah et al[20] showed that vitamin D significantly decreased TG and TC levels and increased HDL levels. In the weighted mean difference analysis, vitamin D replacement significantly decreased only TG. The authors concluded that vitamin D supplementation could be considered a beneficial adjuvant therapy in managing lipid profile levels, especially in individuals with vitamin D deficiency[20]. The impact of vitamin D can be more significant in overweight and obese individuals. For instance, in a previous study[21], vitamin D deficiency was associated with higher levels of TG and TC and tendency towards an increased level of LDL and decreased HDL plasma level.

This is likely due to extremely high temperatures in most parts of Saudi Arabia, which lead to reduced sun exposure as people stay indoors and rely heavily on-air conditioning. Interestingly, plasma vitamin D levels in the Saudi population were found to be higher in winter than in summer[22,23]. Therefore, it was recommended to maintain adequate vitamin D intake through the year. The geographical variation in vitamin D across the Saudia Arabia may represent another reason to conduct different population studies, in order to help health authorities to achieve the best health strategies. In this study, we aimed to assess the effect of vitamin D supplement on diabetes biomarkers such as HbA1c and fasting blood glucose (FBG), and on other blood biomarkers in individuals with T2DM and vitamin D deficiency[24]. Prior studies have reported conflicting or inconclusive findings; by conducting this study in our local patient population, we aimed to provide novel insights that could help resolve the uncertainties surrounding the use of vitamin D as potential adjuvant therapy for managing individuals with diabetes.

MATERIALS AND METHODS

Study setting and design

This was a descriptive retrospective hospital-based study that included 254 participants. The study population was individuals with diabetes mellitus suffering of vitamin D insufficiency. The records of the participants were obtained between December 2021 and July 2022 at the Security Forces Hospital in Riyadh, Saudi Arabia.

Inclusion criteria

- Both genders.
- Age ≥ 18 years.
- Individuals with T2DM.
- Individuals with vitamin D insufficiency.
- Individuals who received vitamin D supplements for at least three months with no change in their antidiabetic medications. We wanted to ensure that vitamin D supplementation was the primary factor driving any observed changes in glycemic control, rather than potential confounding effects from adjustments to antidiabetic medications. By requiring a minimum 3-month period of stable antidiabetic therapy during the intervention, we can be more confident that improvements in outcomes, if observed, are attributable to the vitamin D supplementation rather than changes in concurrent treatments. Furthermore, given the chronic and progressive nature of type 2 diabetes, it is not uncommon for patients to experience adjustments to their antidiabetic regimens over time, even in the absence of any new interventions. By focusing on stability during the study period itself, we believe we can better isolate the specific effects of vita-

min D supplementation, which is the primary objective of our research. This approach aligns with the primary objective of our study, which is to evaluate the specific impacts of vitamin D supplementation on glycemic control and other cardiometabolic parameters such as lipid profile. Maintaining stable antidiabetic and lipid lowering medication management during the intervention period helps us better isolate the effects of vitamin D intervention, which is the key focus of our research.

Exclusion criteria

- Age < 18 years.
- Non-Saudi ethnicity.
- Pregnant.
- Individuals with renal or hepatic disease.

Operational definition of vitamin D insufficiency[25]

- Severe vitamin D deficiency: < 25 nmol/l or 10 ng/ml.
- Vitamin D deficiency: < 50 nmol/l.
- Optimum levels: should be above 50 nmol/l.
- The higher limit for optimum levels is 125 nmol/l

Data collection and study variables

Data collection sheet was used to collect data about on age, gender, weight, body mass index (BMI), fasting blood glucose (FBG), glycated hemoglobin (HbA1c), vitamin D, low-density lipoproteins (LDL), high-density lipoprotein (HDL), triglycerides (TG), total cholesterol (TC), creatinine (Cr), alanine aminotransferase (ALT), aspartate aminotransferase (AST), white blood cells (WBC), red blood cells (RBC), hemoglobin (Hgb), hematocrit (Hct) and thyroid stimulating hormone (TSH). Data was obtained from the electronic medical records of the selected patients. All the above information was collected for each participant in two different times: in baseline (before receiving vitamin D supplements) and after three months of starting vitamin D supplements. Vitamin D (D-Seul) 50,000IU was provided to the participants. The entire study population was using gliclazide and metformin.

Sample size and sampling method

All patients who met the selection criteria during the study period were included, resulting in a sample size of 254 participants.

Ethical approval

The study was approved by the Institutional Review Board of the Security Forces Hospital with protocol research number 23-649-13 on 22/6/2023.

Statistical analysis

Data analysis was performed using SPSS 27 (IBM Corp., Armonk, NY, USA). For the descriptive analysis, mean ± standard deviation (SD) was presented for continuous variables; while counts and percentages (%) were presented for the categorical variables. All continuous variables were tested for normal distribution. Paired sample *t*-tests were conducted to assess the differences in collected data of blood biomarkers between two different times (before and after receiving vitamin D supplements), while an independent sample *t*-test and One-Way ANOVA were used to compare the average vitamin D level among the demographics' groups of study population at baseline. McNemar test was used to determine the association of the categorical variables before and after receiving vitamin D supplementation (50,000 units once weekly for 12 weeks). Pearson correlation was used to determine if there is a correlation between the participants' weight and vitamin D level. The statistical significance of all tests was set at $p < 0.05$.

RESULTS

Baseline characteristics of the participants

This study included 254 patient records for individuals with T2DM and vitamin D deficiency who received vitamin D supplements for at least 3 months with no change in their antidiabetic medications. 97 (38.2) patients were females and 157 (61.8) were males. The average age of the participants was 56.2 ± 8.12 years and 160 (63%) of them were 40-60 years. The mean weight ± SD of the participants at baseline was 80.4 ± 12.4 kg, and for BMI, it was 29.4 ± 4.1 kg/m^2. 162 (63.8%) of them were overweight, while only 12 (4.7%) of participants were normal weight in accordance with the guidelines of the World Health Organization (WHO)[25]. An independent sample *t*-test and One-Way ANOVA showed no significant differences in vitamin D levels among socio-demographic groups. Interestingly, this excluded these factors as confounding variables (Table I).

Vitamin D level, glycemic parameters and lipid profile before and after receiving vitamin D supplement

The mean vitamin D ± SD level before receiving vitamin D supplement was 45.4 ± 5.2 nmol/L, while it was 65.5 ± 5.2 nmol/L after receiving it. Furthermore, the mean HbA1c ± SD before receiving vitamin D supplement was 8.9 ± 0.8 %, while it was 7.8 ± 0.8% after receiving it. The mean FBG before receiving vitamin D supplementation was 10.1 ± 1.5 mmol/L, while it was 8.9 ± 1.5 mmol/L

Table I. Baseline characteristics of the study participants (n=254).

Socio-demographic characteristic	Responses	Total [Mean ± SD or n (%)]	Vit D level at baseline	*p*-value
Gender	Male Female	157 (61.8) 97 (38.2)	45.6 ± 5.1 45.1 ± 5.5	0.246
Age	Mean (SD)	56.2 ± 8.12	–	0.051
Age groups	< 40 Y 40-60 Y > 60 Y	12 (4.7%) 160 (63%) 82 (32.3%)	47.1 ± 2.7 46.3 ± 4.1 43.3 ± 6.7	
Weight (kg)	Mean (±SD)	80.4 ± 12.4	0.045*	0.480
BMI	Mean (±SD)	29.4 ± 4.1	–	0.054
BMI classifications	Normal Over Weight Obese	12 (4.7%) 162 (63.8%) 80 (31.5%)	41.8 ± 6 45.7 ± 5.2 45.4 ± 5.1	

SD = Standard deviation, kg = kilo grams, Y = year, BMI = Body mass index, and n = number. *Correlation coefficient.

after receiving it. The mean LDL level was 4 ± 0.5 mmol/L before receiving vitamin D supplementation, while it was 3.5± 0.4 mmol/L after receiving it (Figures 1, 2, 3A and B, and Figure 4).

When the McNemar test was completed to compare the vitamin D level, glycemic parameters and lipid profile before and after receiving vitamin D supplementation, we found that 247 (97.2%) out of 254 patients with vitamin D deficiency at baseline achieved sufficient vitamin D level (p<0.001). 1 (0.4) out of 254 patients achieved controlled HbA1c after receiving vitamin D supplementation. Regarding FBG, 25 (10.2) out of 254 patients reached FBG controlled level after receiving vitamin D supplementation. Furthermore, only 1 (0.4) out of 254 patients reached controlled LDL level after receiving vitamin D supplementation. Interestingly, 74 (55.6%) patients out of 103 patients with uncontrolled HDL obtained controlled HDL after receiving vitamin D supplementation while 86 (34.7%) patients out of 248 patients with uncontrolled TC obtained controlled TC after receiving vitamin D supplementation (Table II).

Comparisons of all parameters investigated before and after receiving vitamin D supplement

A pairwise comparison using paired sample *t*-test showed that the mean vitamin D level was increased by +19.6 nmol/L after receiving vitamin D supplementation revealed statistically significant result (CI, 19.1- 20.1, $p < .001$). Furthermore, the mean HbA1c decreased by -1.05% after receiving vitamin supplementation, [CI, -(1.01-1.08)%, $p < 0.001$]. In addition, the mean difference in FBG level before using vitamin D supplement and after using it was -1.2 mmol/L, where the level was significantly lowered [CI, -(1.1-1.3), $p < 0.001$]. Unfortunately, all participants (100%) in the pre-intervention period had poor glycemic control (HbA1c ≥ 7%), according to the criteria of

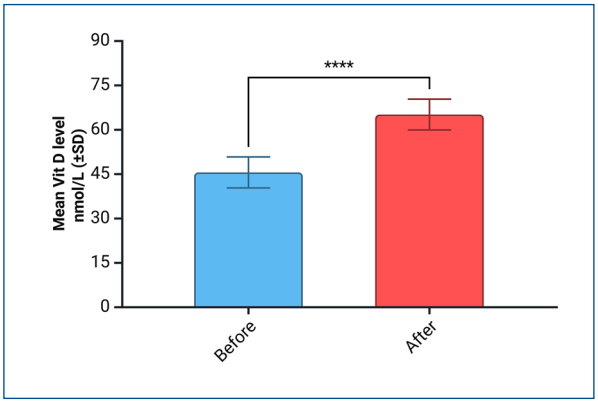


Figure 1. Comparison of the average level of vitamin D level (±SD) among the participants before and after receiving vitamin D supplement (n=254). ****p-value <0.001; p-value of less than 0.05 is considered statistically significant.

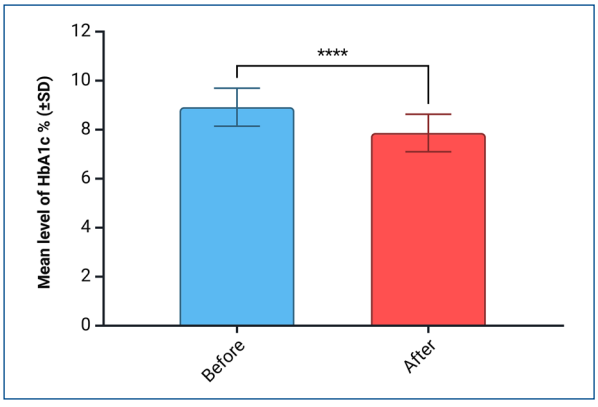


Figure 2. Comparison of the average level of HbA1c level (±SD) among the participants before and after receiving vitamin D supplement (n=254). ****p-value <0.001; p-value of less than 0.05 is considered statistically significant.

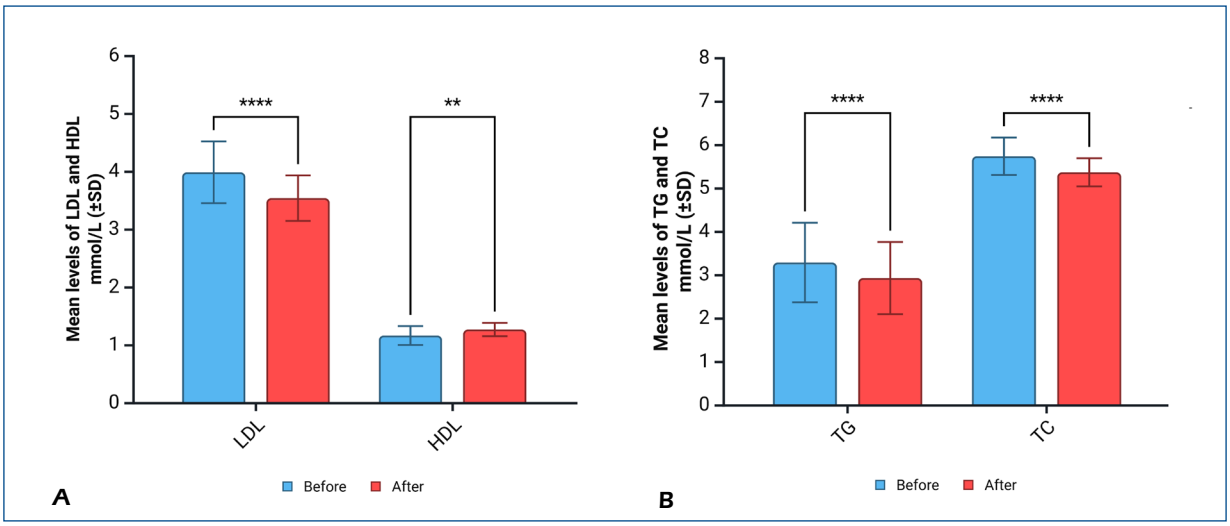


Figure 3. A-B, Comparison of the average levels (±SD) of lipid profile among the participants before and after receiving vitamin D supplement (n=254). ****p-value <0.001; **p-value <0.01; p-value of less than 0.05 is considered statistically significant.

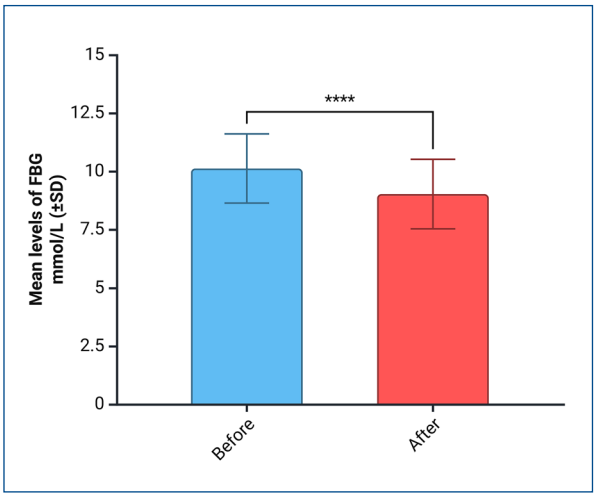


Figure 4. Comparison of the average levels (±SD) of FBG level among the participants before and after receiving vitamin D supplement (n=254). ****p-value <0.001; p-value of less than 0.05 is considered statistically significant.

the American Diabetes Association (ADA)[26]. For lipid profile biomarkers (LDL, HDL, TC, and TG), mean differences in their levels before receiving vitamin D supplement and after were -0.45 mmol/L, +0.10 mmol/L, -0.37 mmol/L, and -0.37 mmol/L, respectively, with statistically significant differences for each biomarker (p < 0.001). Similarly, the levels of all other investigated blood biomarkers was significantly different after taking vitamin D supplement (their mean differences were as follows: Cr: -3.8 µmol/L, ALT: -3.4 U/L, AST: -3.4 U/L, WBC: -0.28, RBC: +0.24, Hgb: +22.7 g/l, Hct: +0.039 L/L and TSH: +0.25 mIU/L) (p < 0.001) (Table III).

DISCUSSION

This study showed that supplementation of vitamin D was associated with potential improve-

Table II. Exploration of the improvement of the vitamin D level, glycemic parameters and lipid parameters before and after receiving vitamin D supplement among participants (n=254).

	Total numbers of patients with uncontrolled parameters before receiving vitamin D- (N)	Number of patients with uncontrolled/parameters that got controlled after receiving vitamin D - N (%)	p-value
Vit D Level	254	247 (97.2)	<0.001
HbA1c	254	1 (0.4)	–
FBG	254	25 (10.2)	–
LDL	254	1 (0.4)	–
HDL	133	74 (55.6)	<0.001
TC	248	86 (34.7)	<0.001

Fasting blood glucose (FBG), glycated hemoglobin (HbA1c), Vitamin D (Vit D), low-density lipoproteins (LDL), High-density lipoprotein (HDL), total cholesterol (TC).

Table III. The comparison of blood biomarkers before and after receiving vitamin D supplement in individuals with T2DM.

	Mean ±SD before	Mean ± SD after	Mean difference	SE mean	95% CI of the difference		*p*-value
					Lower	Upper	
HbA1c%	8.9±0.8	7.8±0.8	1.052	0.016	1.019	1.08	<0.001
FBG mmol/L	10.1±1.5	8.9±1.5	1.18	0.039	1.109	1.26	<0.001
Vit D nmol/l	45.4±5.2	65±5.2	-19.58	0.258	-20.09	-19.07	<0.001
LDL mmol/L	4±0.5	3.5±0.4	0.45	0.017	0.417	0.48	<0.001
HDL mmol/L	1.2±0.2	1.3±0.1	-0.104	0.004	-0.11	-.094	<0.001
TG mmol/L	3.3±0.9	2.9±0.8	0.36	0.017	0.33	0.39	<0.001
TC mmol/L	5.7±0.4	5.4±0.3	0.37	0.014	0.34	0.39	<0.001
Cr µmol/L	63.6±6.9	59.7±6.2	3.83	0.180	3.47	4.18	<0.001
ALT U/L	22.9±3.7	19.4±3.5	3.44	0.066	3.31	3.57	<0.001
AST U/L	22.2±3.5	18.8±3	3.40	0.081	3.24	3.56	<0.001
WBC	6.7±1.2	6.5±1.2	0.28	0.008	0.26	0.29	<0.001
RBC	4.7±0.5	4.9±0.5	-0.23	0.007	-0.25	-0.22	<0.001
Hgb g/L	132.2±8.8	154.9±8.1	-22.67	0.427	-23.5	-21.83	<0.001
Hct L/L	0.4±0.02	0.5±0.02	-0.03	0.001	-0.04	-0.037	<0.001
TSH mIU/L	2.9±0.5	3.1±0.5	-0.24	0.005	-0.25	-0.23	<0.001

Fasting blood glucose (FBG), glycated haemoglobin (HbA1c), Vitamin D (Vit D), low-density lipoproteins (LDL), high-density lipoprotein (HDL), triglycerides (TG), total cholesterol (TC), creatinine (Cr), alanine aminotransferase (ALT), aspartate aminotransferase (AST), white blood cells (WBC), red blood cells (RBC), haemoglobin (Hgb), haematocrit (Hct) and thyroid stimulating hormone (TSH). SD = Standard deviation, and SE = Standard error.

ment in HbA1c, FBG, all parameters of lipid profile, renal and liver function and hemoglobin ($p < 0.001$). In this study, we used HbA1c as a maker for detecting glycemic changes before and after vitamin D supplementation[24,27]. Vitamin D is linked to the pathophysiology of T2DM; however, its exact method of action is unknown. The synthesis, resistance, sensitivity, and action of insulin are all directly impacted by vitamin D[28-30]. With these actions, vitamin D contributes to the control of the body's glycemic state (HbA1c). Importantly, it was shown that in a Saudi population, vitamin D was inversely linked to HbA1c and FBG levels[31]. Additionally, vitamin D typically has immunomodulatory and anti-inflammatory properties[32,33]. Al-Quaiz et al[34] reported that vitamin D deficiency is considered as a risk factor for diabetes and dyslipidemia. In our study, we found positive effects for the vitamin D supplements on main diabetic markers (HbA1c and FBG), and on all other blood biomarkers investigated. This finding indicates the potential importance of vitamin D in controlling diabetes and its role in improving other blood biomarkers that are important in body health. Abukanna et al[9] showed in a systematic review different impacts of vitamin D on glycemic control and lipid profile and that more research is needed in this area. Our study supports the notion that vitamin D supplement is associated with improvement in glycemic control. The high level of plasma Vitamin D level can be seen during the winter in Saudi population and low levels in summer[22,23]. Although sunlight is a well-known source of vitamin D, approximately 80% of Saudis with type 2 diabetes mellitus (T2DM) were reported to have low levels of sun exposure[35]. Sun exposure among the Saudi population with type 2 diabetes was also found to be low during Ramadan[36]. In addition to the hot weather particularly during the summer, the consciousness of the harmful effects of sun exposure, including ageing and skin cancer, were found as barriers that limit Saudis' exposure to the sun[37,38]. Therefore, oral vitamin D supplement may be another important mean of treating vitamin D deficiency in Saudi population. Zhang et al[10] showed that long term oral supplementation of vitamin D can be associated with improvement in insulin resistance. Further research is needed to assess whether (i) long term supplementation will be needed in Saudi population in order to achieve adequate glycemic control, (ii) whether such supplementation with vitamin D may lead to decrease in cardiovascular disease, (iii) whether geographical location may determine the duration of vitamin D supplement, and (iv) whether vitamin D may decrease overall mortality and complications associated with diabetes.

In addition, this study found that improving vitamin D levels was associated with lower TC, TG, and LDL levels, but higher HDL levels, which are consistent with previous studies[38,39]. In contrast, previous studies have reported converse results, increasing vitamin D failed to improve lipid profiles[40,41]. However, in Sudi population, Alotaibi et al[18] showed that low vitamin D was associated with high LDL-cholesterol. Importantly, deficiency was also found to be associated with dyslipidemia[19]. An umbrella review showed that vitamin D supplementation could be considered beneficial adjuvant therapy in managing lipid profile levels, especially in overweight and obese individuals with vitamin D deficiency[20,21]. Further research is needed to determine whether vitamin D supplementation can be used in the treatment of dyslipidemia. Despite many studies found that vitamin D in Saudi females was lower than in males because females were less sun exposure[41-43], our study did not see a difference between males and females in vitamin D level. Importantly, the role of clinical pharmacists in improving adherence with vitamin D supplementation in individuals with type 2 diabetes can be subject for future studies, especially during Ramadan[7,44-48]. It is not yet clear how vitamin D supplement plays a role in diabetes control, but there are some explanations of how vitamin D affects glycemic control in individuals with diabetes. One of these explanations is that the majority of the cells, such as the pancreatic β-cells, are comprised of vitamin D receptors, that regulates paracrine and intracrine functions[28,30]. The molecular and pathophysiological relationship between Vitamin D and insulin resistance is complex[49,50]. However, several mechanisms may explain this finding:

1) vitamin D increases the expression of insulin receptors in different parts of the body like liver, muscles and adipose tissues;
2) low vitamin D leads to an increase in pro-inflammatory cytokines, and this may also increase risk of insulin resistance in conditions regarded as chronic inflammation, such as obesity and fatty liver;
2) vitamin D supplements can decrease leptin hormone, and this may decrease weight and inflammation;
4) vitamin D binds directedly to vitamin D receptors and helps pancreatic β-cells in releasing insulin, or indirect mechanism as vitamin D increase calcium entry into the β-cells and release of insulin;
5) polymorphism of vitamin D rectors (4 were genetically identified) are associated with insulin resistance;
6) vitamin D also helps as antiviral, promotes cell survival and maintains immunity.

The presence of polymorphism of vitamin D receptors may explain in part why some studies showed conflicting outcomes with vitamin D supplements or may necessitate the need for more research to understand why some individuals, despite normal vitamin D level, still develop diabetes. Han et al[51] showed, in a meta-analysis that included a total of 28 articles based on four gene variations namely *TaqI*, *BsmI*, *ApaI*, and *FokI* variants, an association between insulin resistance-related diseases like metabolic syndrome, fatty liver and type 2 diabetes and the VDR *ApaI* variant in Asians and populations who lived in middle-latitude districts. The *BsmI* (mostly A allele than G allele) and *TaqI* variants (T/C allele) were more prevalent in dark-pigmented Caucasians. Furthermore, there was no association between the VDR *FokI* variant and insulin resistance-related diseases in populations with different skin pigments and in different latitudes[51]. Therefore, conduction of large longitudinal prospective studies with genetic studies in Saudi Arabia may reveal an enhance our understanding about the relationship of vitamin D and glucose and lipid metabolism.

Strengths and limitations

This study included the important diabetics biomarkers (HbA1c and FBG) and many other blood biomarkers, such as lipid profiles in a group of Saudis with T2DM. A limitation of the study is that the observed improvements in the investigated variables may be attributed to lifestyle changes, such as increased physical activity or dietary modifications, rather than solely to vitamin D supplementation. However, the findings would be more robust and informative if additional clinical information, such as physical activity, duration of diabetes, patients' weight, and sun exposure, had been available and included in the study. This would have allowed for an assessment of the potential impact of these confounding factors. Further large prospective populations studies from different cities from Saudi Arabia are needed before generalization of this result to all population in Saudi Arabia.

CONCLUSIONS

The study supports the previous observations that vitamin D supplement has potential to improve glycemic control and lipid profile in the Saudi population. In view of the limitations of this study, a large prospective population study with recruitment of participants from different regions in Saudi Arabia during summer and winter will provide accurate evidence of the impact of vitamin D in glycemic control and lipid profile in the Saudi population.

Ethics Approval and Consent to Participate
The study protocol was reviewed and approved by the research committee in Security Forces Hospital, which is constituted and functions in accordance with the National Committee of Bio Ethics (NCBE) in Saudi Arabia, accreditation number (H-01-R-069). Security Forces Hospitals are known as teaching and research organization and patients were consented for such purpose and their data will be kept anonymous. The study was approved by the Institutional Review Board of the Security Forces Hospital with protocol number 23-649-13 and the date was [22/6/2023].

Availability of Data and Materials
The data sets used and/or analyzed during this study are available from the corresponding author on request.

Conflicts of Interest
The authors declare that they have no competing interests.

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Authors' Contributions
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